

(19) (KR)
(12) (A)

(51) Int. Cl.⁷
C07D 215/14
C07D 405/06

(11)
(43)

10-2004-0081161
2004 09 20

(21) 10-2004-7011808

(22) 2004 07 30

2004 07 30

(86) PCT/EP2003/000954

(87)

WO 2003/064392

(86) 2003 01 30

(87)

2003 08 07

(30) 60/353,787 2002 01 31 (US)

(71) -4056 35

(72) , -4052 53

, -68330 44

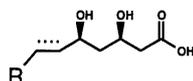
(74)

:

(54) HMG - C o A

I , ,

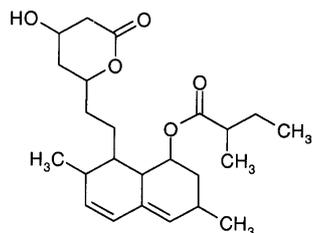
< I >



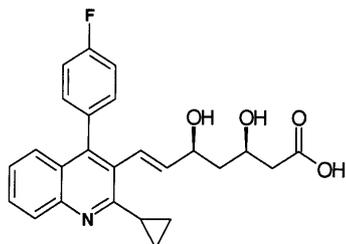
----- -CH₂-CH₂- -CH=CH-

R

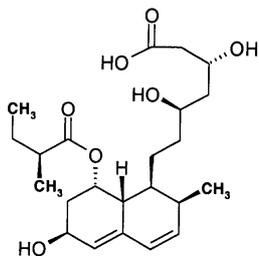
HMG-CoA , , , , ,



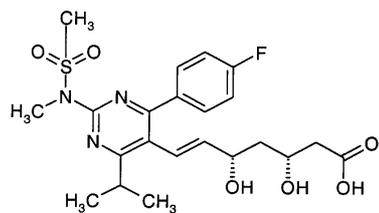
5,856,336



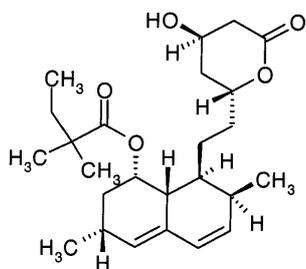
4,410,629



5,260,440



4,444,784



dex)

(LifeCycle Patents International) , IMS

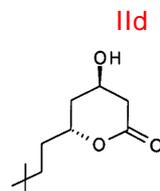
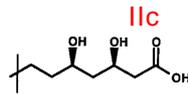
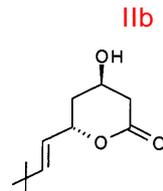
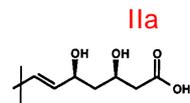
(Patents International)

(IMS World Publications)

(The Merck In

HMG-Co-A

la (3,5-
IIC -6-
(3,5-) IId



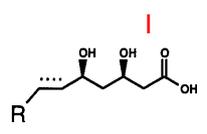
가 IIa IIc , 3,5-syn C-3 R-

I

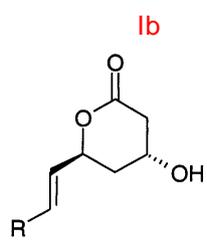
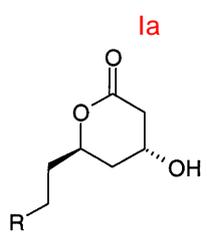
가

(Wittig-Wadsworth-Emmons ((Wittig-Horner))) (Wittig)
 99.5 % 99 % ee 99 % , 95 % , (ee) 98 % , 가
 , 95 % , 98 % , 가
 (de)

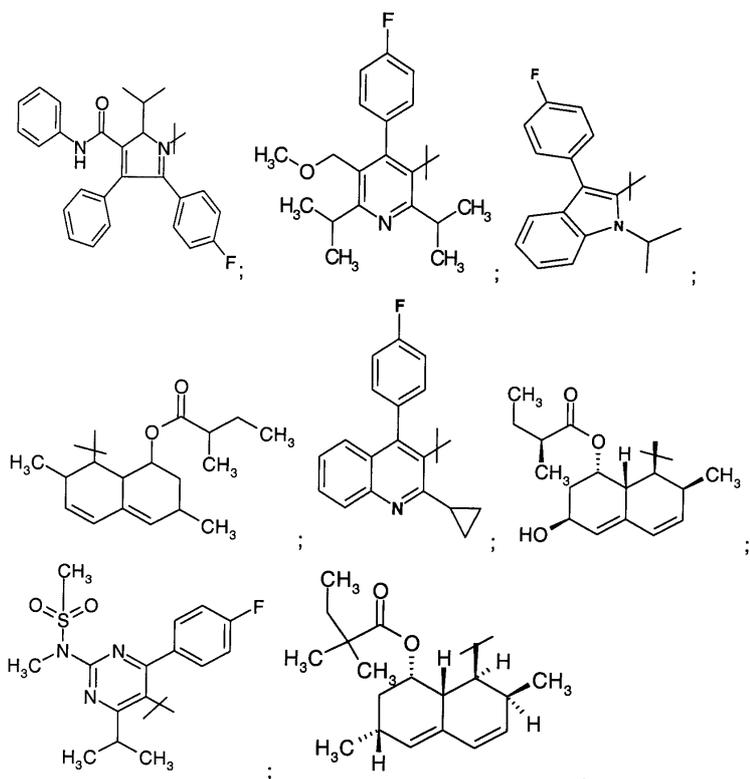
I HMG-CoA



----- -CH₂-CH₂- -CH=CH-
 R
 I
 I la lb



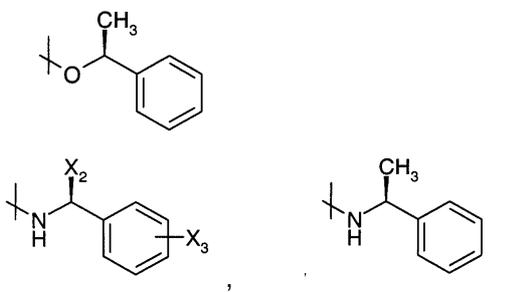
R



가 ,

[J.Org.Chem. 1991, 56, 3744-3747]
N- N₂O₄

, (ii) , 가 , (iii) (i)



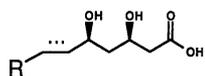
[Bioorg. Med. Chem. Lett. 9 (1999) 2977-2982]

IIa

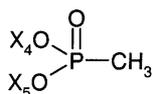
1/2

(a) IIIa IIIb
IIIc

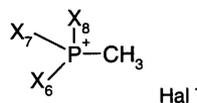
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IIIa

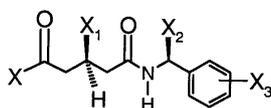


IIIb



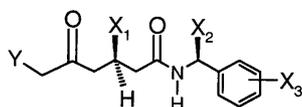
(
 X_4 , X_5 , C_1-C_7 - , $-C_1-C_7$ - ,
 X_6, X_7 , X_8 , CF_3 , C_1-C_7 , , C_1-C_7 , C_2-C_8 - ,
 Hal -)

IIIc

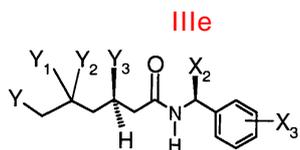


(
 X , , - 2 ,
 X_1 , ,
 X_2 , C_1-C_7 , ,
 X_3 , CF_3 , C_1-C_7 , , C_1-C_7 , C_2-C_8 - , ,
 (b) , , IIIc IIIe

IIIc



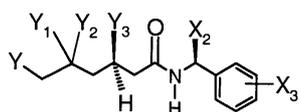
(
 X_1, X_2, X_3
 $Y (X_4 O)(X_5 O)P(=O)- (X_6)(X_7)(X_8)P + Hal^-$
 $X_4, X_5, X_6, X_7, X_8 Hal^-$)



(
 $X_2, X_3 Y$
 $Y_1, Y_2, Y_3, Y_1 Y$
 $Y_3 syn-$
 $Y_1 Y_3 -O-Alk-O-, Alk C_1-C_7, Y_2, Y_1 Y_3 syn-$

(c) **IIIe** **IIIg** **IIIg**
 ----- 가 -CH=CH- ----- 가 -CH₂=CH₂-

< **IIIe**>

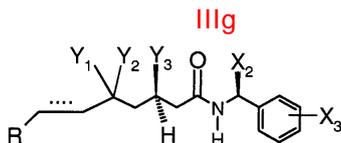


(
 $X_2, X_3 Y$
 Y_1, Y_2, Y_3, Y
 $Y_1 Y_3 syn-$
 $Y_1 Y_3 -O-Alk-O-, Alk C_1-C_7, Y_2, Y_1 Y_3 syn-$
 $Y_1 Y_2, Y_3, IId$
)

< **IIIg**>

R-CH(=O)

(
 R)



(,

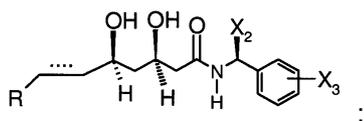
R ,

X_2, X_3, Y_1, Y_2, Y_3 ,

----- -CH₂-CH₂- -CH=CH-);

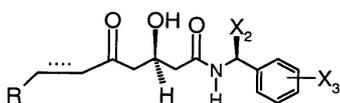
(d) Y_1, Y_3 , Y_2 , Alk C₁-C₇ , Y_1, Y_3 syn , Y_1, Y_3 syn ; Y_1, Y_3 -O-Alk-O-IIIg , Y_2 , 가 .
 ----- 가 -CH=CH- IIIh () , IIIh ----- 가 -CH₂-CH₂- IIIh , 가 .

< IIIh >



(e) Y_1, Y_2 가 =O IIIh Y_3 IIIg (X₁) IIIi IIIg , II
 li IIIh

< IIIi >

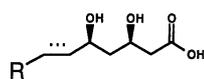


(,

R, X_2, X_3 ----- 가);

(f) IIIh I 가

< I >



(,

----- -CH₂-CH₂- -CH=CH- ,

R)

(g) I, I la, Ib, I la, Ib, IIIc, IIIc''', IIIc''''
 , X₂, X₃, HMG-CoA

가 C₁-C₇, -C₁-C₇, C₃-C₈, C₃-C₈
 R-CO-O, C₂-C₈, -C₂-C₈

- 2-, C₃-C₈-2-, C₁-C₇, C₁-C₇, -C₁-C₇, C₃-C₈-
 C₁-C₇, tert-가, n-, n-, C₁-C₄가, sec-

C₁-C₇, n-, n-, sec-, tert-
 C₁-C₄

C₃-C₈, -C₁-C₇, C₃-C₈, C₃-C₈
 C₃-C₆

C₃-C₈, C₃-C₆

C₂-C₈, -C₂-C₈, C₂-C₅

가 35

-C₁-C₇, -C₁-C₄, 1-, 2-
 C₁-C₇, 2,2-, 3,3-, C₂-C₅, 1,1-, 2,2-, 1,1-, 2,2-, 1,1-
 (X₂ () X₄)
 -C₁-C₇, tert-

C₁-C₇, C₁-C₄, 1,2-, 1,2-, 1,3-
 C₂-C₇, 2,2-가, C₂-C₄, 1,1-, 1,1-, 2,2-

(ar)
 , C₂-C₈, 2, 3, CF₃, C₁-C₇, C₁-C₇

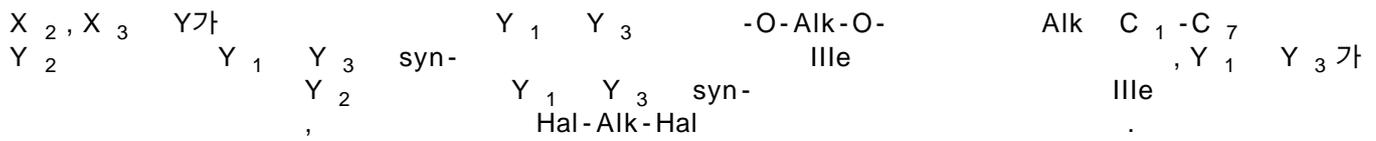
() -10 +200 가 , -80

(a):

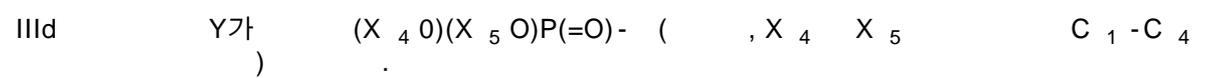
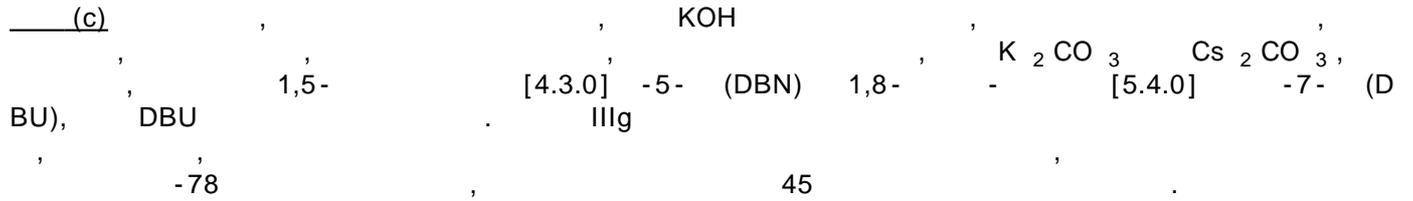
(a) IIIa IIIb , -78 0 , -78 , IIIc 가 , -78
 X C₁-C₇ N- -N- , N-C₁-C₇ -N-C₁-C₇ ,가
 IIIc X가 N-C₁-C₇ -N-C₁-C₇ ,가 N- -N-

(b):

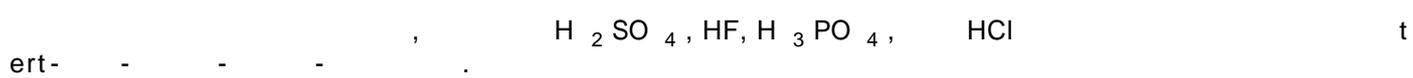
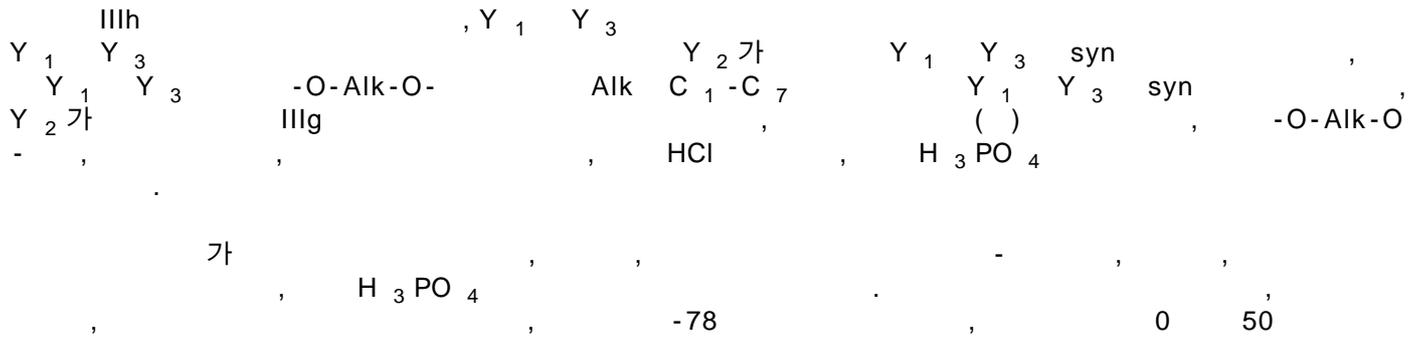
X₄ X₅ C₁-C₇ , C₁-C₄ ,가
 X₆, X₇ X₈
 Hal -
 IIIa
 X₂, X₃ Y , Y₁ , Y₂ , Y₃
 , Y₁ Y₂가 , Y₁ Y₃ syn-IIIe IIIe
 (Ru(cod)(nu-3-(2-₁ 3)))₂
 가 가 ()
 -C₁-C₇ -C₁-C₇ ,가
 -78 , -78 0 ,
 0 , 20 50 ,
 , Y₁ Y₁-Hal Y₂가 IIIe , Y₁ ,



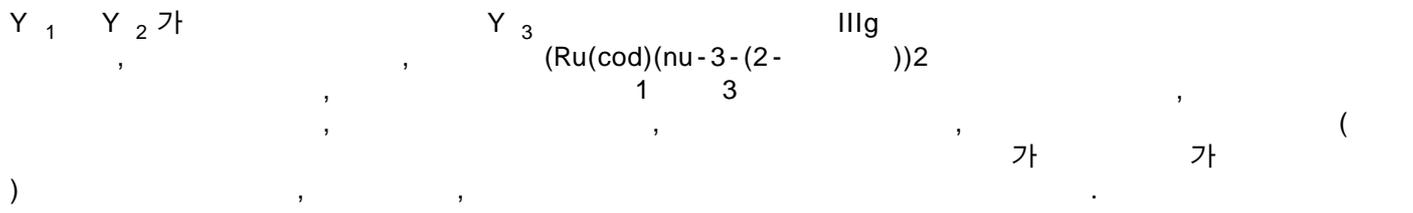
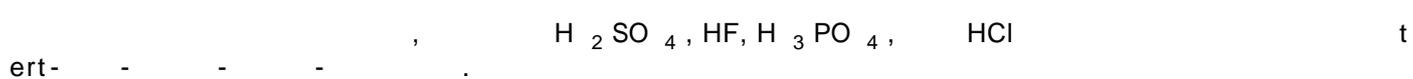
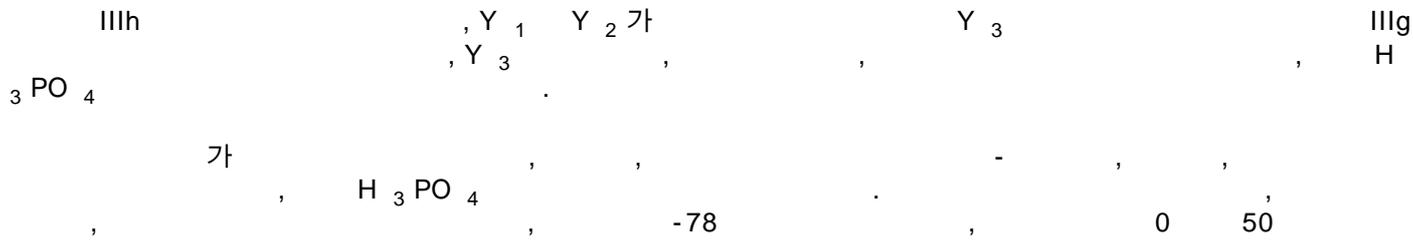
____(c):



____(d):



____(e):



-C₁-C₇ -C₁-C₇ - , 가 -

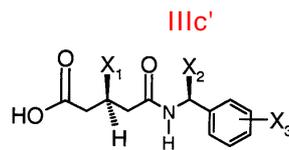
-78 0 , -78 ,
0 , 20 50 ,

____(f):

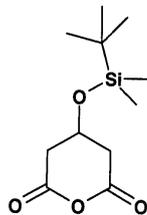
가 _____(f) , IIIg , Na
OH , Ca(OH)₂ ,

____(g):

I _____(g) I
IIIc , IIIc'

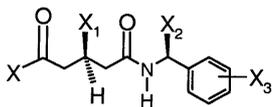


2 1-

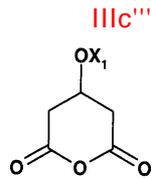
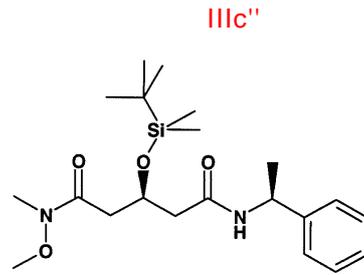


IIIc'''
N-C₁-C₇ -N-C₁-C₇ - (1) IIIc''''
IIIc , N- -N- - IIIc''''

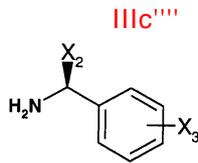
< IIIc >



X N-C₁-C₇ -N-C₁-C₇ - , N- -N- -



X₁ , tert- - .



X₂ X₃ .

N-C₁-C₇ -N-C₁-C₇- - , N- -

IIIc IIIc , X가 N-C₁-C₇ -N-C₁-C₇- - , N- -N- -
(subject matter) .
가

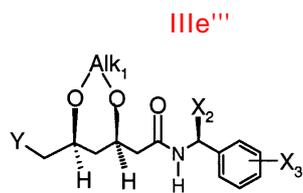
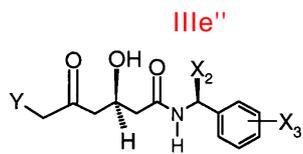
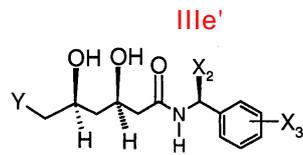
X가 N-C₁-C₇ -N-C₁-C₇- - , N- -N- - IIIc

, -N- - X가 IIIc N-C₁-C₇ -N-C₁-C₇- - ,가 N-
, X₁ - 가 (a) - .

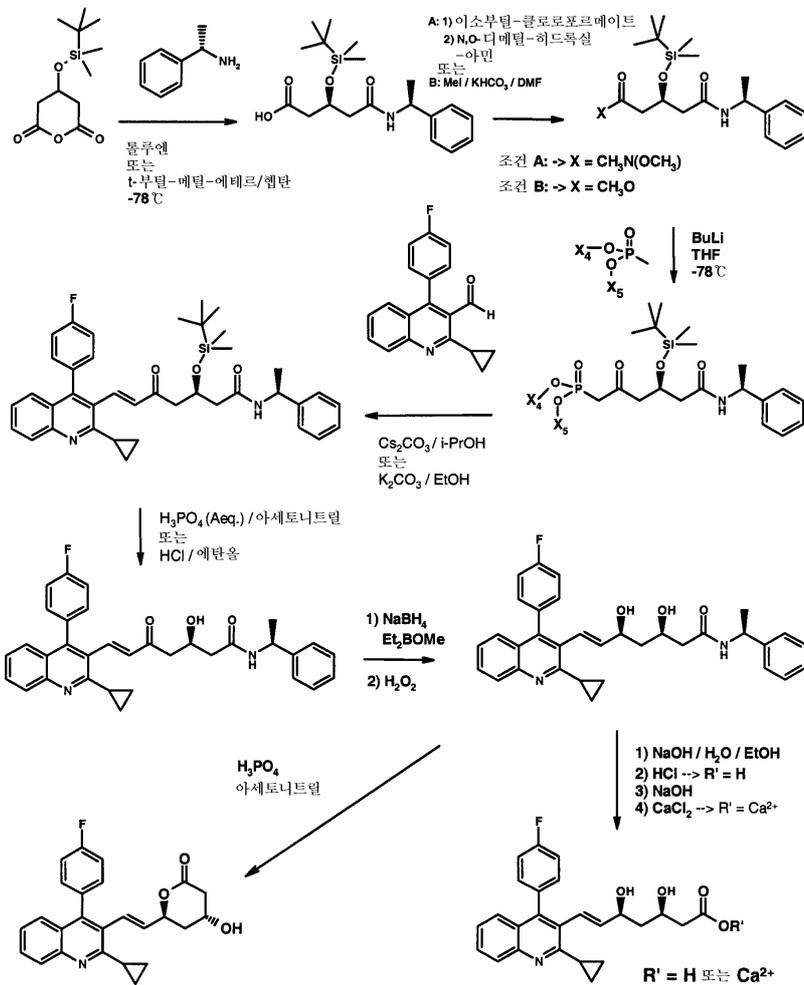
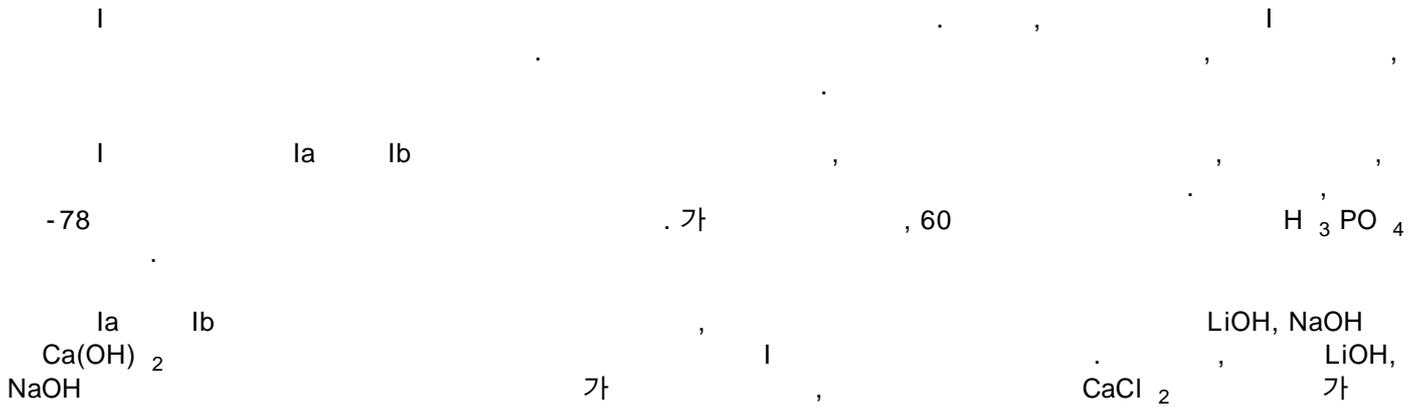
, - 가

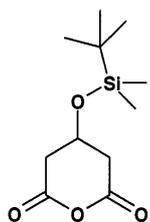
, -N- - X가 IIIc N-C₁-C₇ -N-C₁-C₇- - (b) ,가 N-
가 ,

가
 III d , X₁ , tert-
 Y₃ , tert- III e
 Y₃ , tert- III e
 (c) 가 , 가
 III e III e', III e'' III e'''



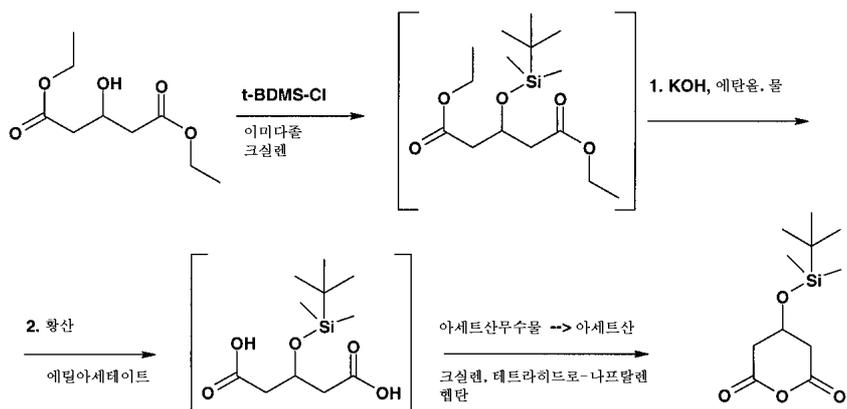
Alk₁ 1- -1,1-
 III e', III e'' III e'''
 III g , Y₃ , tert-





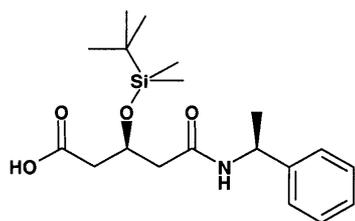
3-(tert-butyl dimethylsilyloxy) succinic anhydride (Aldrich)

3-(tert-butyl dimethylsilyloxy) succinic acid



100 g (107.5 g, 0.5 mol), (44.2 g, 0.6 mol) 4 (200 Mℓ) 3- (84.1 g, 0.55 mol) 7
 80 가 , (100 Mℓ) t- 30 40
 가 , 6 70 80
 (200 Mℓ) 가 (100 Mℓ)
 , (95 %, 200 Mℓ) (119.8 g, 49.2 %, 1.05 mol) 가 10
 20 15 25 , (1200 Mℓ) (300 Mℓ) 가
 . (230 Mℓ, 20 %) 0 15 pH
 3.0 3.5가 가 (15 20 가 ,
 (200 Mℓ) . (100 Mℓ) (200 Mℓ) 가
 , , 60 70 (200-60 mbar) 1/2
 , (103.5 g, 1.0 mol) 55 65 20 40 가 , 2 4
 (80 , 100 20 mbar) . (600 Mℓ) 30
 40 가 , -15 , 1 . 58 68
 , (100 Mℓ) , (60 , 10 20 mbar)
 , 80 82

2



(3S,1'S)-3-[(tert-butyl dimethylsilyloxy)methyl]-5-[(1S)-1-phenylethylamino]pentanoic acid
 sky, Mary F. Malley and Jack Z. Gougoutas, J. Org. Chem. 1991, 56, 3744-3747]

[Donald. S. karanew

(Karanevsky)

(hindered base), N

(S)-(-)-1-

2 mol (S)-(-)-1-

1 mol

1 mol

(3S,1'S)-3-[(tert-)]-5-[(1-

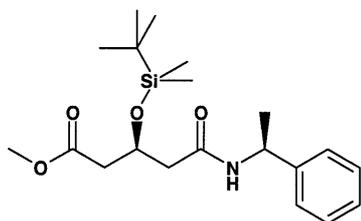
98 %

(de) 98 %

(ee) 가

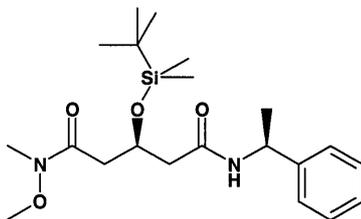
30 g, 0.123 mol) t- (210 Ml) 가 4 () () ()
 (120 Ml) (S)-(-)-1- (120 Ml) -78 () () ()
 90 가 (31.3 g, 0.258 mol, 99.6 % ee) -78/-75 60
 (100 Ml) 가 , 30 35 가 , pH 2.5 3.5가 ()
 100 Ml, 20 %) 가 (70), 30
 0 5 / (1:1) (80 Ml), (20 %, 100 Ml)
 70 172 (50 60 , 10 20 mbar) 1
 -5- 98 % de 98 % ee 가)]-5-[(1- -)]

3



(3S,1'S)-3-[(tert-)]-5-[(1- -)]-5-

4



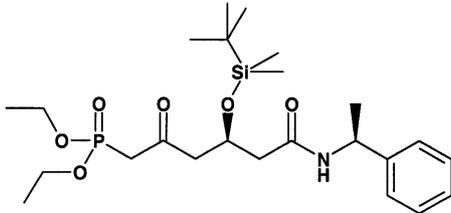
(S)-3-(tert- - -)- - - -((S)-1- - -)

27.36 mmol) (200 Ml) . N- 가 4 () (2) (10 g, 가
 -20 (6.03 Ml, 54.71 mmol) 가
 w/w , 27.36 mmol) -15 -20 (3.76 Ml, 95 %
 , N,O- 가 15 -15 -20
 가 (2.695 g, 27.36 mmol) 1
 , (200 Ml)

MgSO₄ (2 x 200 Mℓ) (S)-3-(tert-butylamino)-5-oxo-1-phenylpentan-2-one (200 Mℓ)
 (S)-3-(tert-butylamino)-5-oxo-1-phenylpentan-2-one
 M.p. 69.6-70.1 °C; [α]_D²⁰ = -27° (CHCl₃, c=1); MS (ES+, m/z): 431([M+Na]⁺, 100 %); IR(KBr): 3304, 1666, 1630, 1541, 831 cm⁻¹

< 1 >

a)

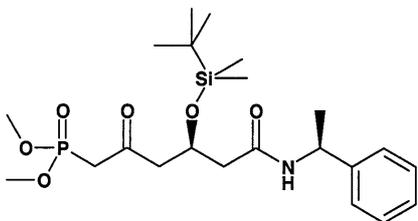


[(R)-4-(tert-butylamino)-2-oxo-5-((S)-1-phenylethylamino)pentan-1-yl diethylphosphine oxide]

(4.65 g, 30.59 mmol) (11 Mℓ) -78 (10 g)
 1.6 M 15.3 Mℓ, 24.47 mmol 가 -78 60 (S)-3-(tert-butylamino)-5-oxo-1-phenylpentan-2-one (2.5 g)
 Mℓ 가 (1.25 Mℓ) 가 (1.84 g) 가
 가 (125 Mℓ) (125 Mℓ) 10
 [(R)-4-(tert-butylamino)-2-oxo-5-((S)-1-phenylethylamino)pentan-1-yl diethylphosphine oxide]
 / (1:1) [(R)-4-(tert-butylamino)-2-oxo-5-((S)-1-phenylethylamino)pentan-1-yl diethylphosphine oxide]
 Mℓ [α]_D²⁰ = -40.2° (CHCl₃, c=1); MS (ES+, m/z): 522 ([M+Na]⁺, 100 %); IR (KBr): 3297, 2930, 1717, 1652, 1542, 1254, 1026, 837 cm⁻¹

[(R)-4-(tert-butylamino)-2-oxo-5-((S)-1-phenylethylamino)pentan-1-yl diethylphosphine oxide]
 (S)-3-(tert-butylamino)-5-oxo-1-phenylpentan-2-one
 (3S,1'S)-3-[(tert-butylamino)amino]-5-oxo-1-phenylpentan-2-one

b)

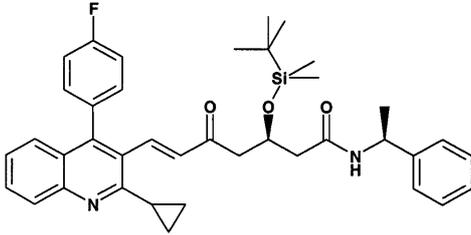


[(R)-4-(tert-butylamino)-2-oxo-5-((S)-1-phenylethylamino)pentan-1-yl diethylphosphine oxide]

[(R)-4-(tert-butylamino)-2-oxo-5-((S)-1-phenylethylamino)pentan-1-yl diethylphosphine oxide]
 [(R)-4-(tert-butylamino)-2-oxo-5-((S)-1-phenylethylamino)pentan-1-yl diethylphosphine oxide]

[(R)-4-(tert-butyl)-2-(5-((S)-1-phenylethylamino)-3-(4-(4-fluorophenyl)-3-(cyclopropylidene)quinolin-2-ylidene)but-3-en-2-ylidene)-2-methylpropanoate] sodium salt. $[\alpha]_D^{20} = -37.7^\circ$ (CHCl₃, c=1); MS (ES+, m/z): 494 ([M+Na]⁺, 100 %); IR (KBr): 3299, 2955, 2929, 2855, 1717, 1651, 1542, 1256, 1035, 838, 779, 701 cm⁻¹.

c)



(E)-(R)-3-(tert-butyl)-7-[2-(4-(4-fluorophenyl)-3-(cyclopropylidene)quinolin-2-ylidene)-3-(1-phenylethylamino)but-3-en-2-ylidene]-5-oxo-2-methylpropanoate sodium salt.

[(R)-4-(tert-butyl)-2-(5-((S)-1-phenylethylamino)-3-(4-(4-fluorophenyl)-3-(cyclopropylidene)quinolin-2-ylidene)but-3-en-2-ylidene)-2-methylpropanoate] sodium salt (3 g, 6 mmol) was dissolved in 12 Mℓ of THF. To this solution, (1.96 g, 6 mmol) of sodium acetate and (1.75 g, 6 mmol) of sodium hydroxide were added. The mixture was stirred in 60 Mℓ of THF for 2 hours. The reaction mixture was diluted with 120 Mℓ of THF and extracted with tert-butyl methyl ether (2 x 120 Mℓ). The combined organic phases were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (7:3) to yield (E)-(R)-3-(tert-butyl)-7-[2-(4-(4-fluorophenyl)-3-(cyclopropylidene)quinolin-2-ylidene)-3-(1-phenylethylamino)but-3-en-2-ylidene]-5-oxo-2-methylpropanoate sodium salt. $[\alpha]_D^{20} = -28.8^\circ$ (CHCl₃, c=1); MS (ES+, m/z): 659 ([M+Na]⁺, 100 %); IR (KBr): 1647, 1605, 1540, 1513, 1253, 1223, 1094, 1066, 837, 778, 763, 699 cm⁻¹.

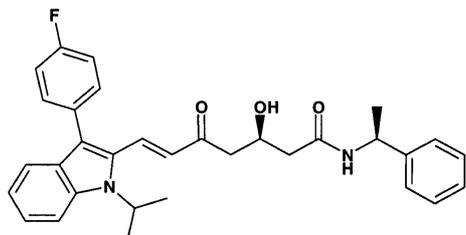
(E)-(R)-3-(tert-butyl)-7-[2-(4-(4-fluorophenyl)-3-(cyclopropylidene)quinolin-2-ylidene)-3-(1-phenylethylamino)but-3-en-2-ylidene]-5-oxo-2-methylpropanoate sodium salt.

[(R)-4-(tert-butyl)-2-(5-((S)-1-phenylethylamino)-3-(4-(4-fluorophenyl)-3-(cyclopropylidene)quinolin-2-ylidene)but-3-en-2-ylidene)-2-methylpropanoate] sodium salt (424.9 g, 910 mmol) was dissolved in 950 Mℓ of THF. To this solution, 119.8 g (858.1 mmol) of sodium acetate and 250 g (858.1 mmol) of sodium hydroxide were added. The mixture was stirred in 1800 Mℓ of THF for 5 hours. The reaction mixture was diluted with 3500 Mℓ of THF and extracted with tert-butyl methyl ether (3500 Mℓ). The combined organic phases were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (70 g) to yield (E)-(R)-3-(tert-butyl)-7-[2-(4-(4-fluorophenyl)-3-(cyclopropylidene)quinolin-2-ylidene)-3-(1-phenylethylamino)but-3-en-2-ylidene]-5-oxo-2-methylpropanoate sodium salt (braun honey).

d)

(7400 Mℓ 2 %) , (5000 Mℓ) , (1800 Mℓ)
 , (2000 Mℓ) , (561.2 g) , (860 Mℓ)
 , n- (1075 Mℓ) 가 , 60 2 , 50 1 가 ,
 n- (1075 Mℓ) 50 가 , , 3
 0
 5- - 6- ((S)-1-)- (E)-(R)-7-[2- -4-(4- -)- -3-]-3-
 n- (502 Mℓ)

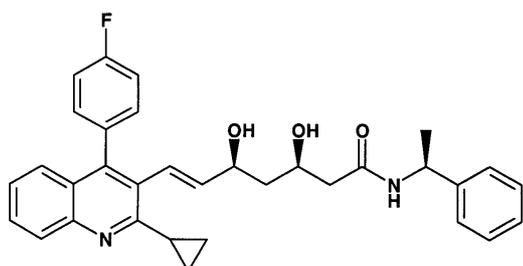
f)



(E)-(R)-7-[3-(4- -)-1- -1H- -2-]-3- -5- - 6- ((S)-1-
 -)- (E)-(R)-7-[2- -4-(4- -)- -3-]-3- -5- -
 -6- ((S)-1- -)- HCl
 (E)-(R)-3-(tert- - -)-7-[3-(4- -)-1- -1H- -2-]-5-
 - 6- ((S)-1- -)- /n- (9:1)

(E)-(R)-7-[3-(4- -)-1- -
 1H- -2-]-3- -5- - 6- ((S)-1- -)- . R_f = 0.30 (
 TLC, / (9:1)). []_D²⁰ = -35.5 ° (CH₃OH, c=1) MS (ES+, m/z):
 535([MNa]⁺, 100 %); IR(KBr): 3307 (), 3061, 2973, 2932, 1645, 1590, 1539, 1495, 1452, 1421, 1
 371, 1339, 1273, 1221, 1155, 1138, 1105, 1095, 1048, 1016, 973, 910, 839, 815, 744, 719, 700 cm⁻¹.
 : C₃₂H₃₃FN₂O₃ (): 74.98 (74.20) % C, 6.49 (6.49) % H, 5.46 (5.49) % N, 3.71 (3.5
 8) % F.

g)



(E)-(3R,5S)-7-[2- -4-(4- -) -3-]-3,5- - 6- ((S)-1-
 -)-
 가 , 3
 (7.5 Mℓ) , -78 , (172.5 mg, 4.56 mmol) 가 ,
 - (50 % 0.694 g, 3.47 mmol) -78 가 , 5
 - [2- -4-(4- -)- -3-]-3- -5- - 6- ((S)-1- -)
 - (1.84 g, 3.52 mmol) -78 30 가 , 1
 (12 Mℓ) (0.383 g)
 (30 Mℓ) 가 , 가 30
 (2 x 30 Mℓ)
 (15 Mℓ)
 0.994 g, 10.23 mmol) 45 50 가 , 45 50 (35 %
 2 가 , 45 50

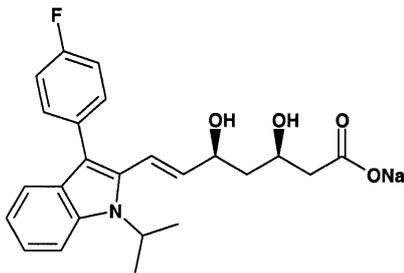
(15 Mℓ) 가
 45 50 Na₂SO₃ (15 Mℓ) 45 50 20 , , 5
 , , NaCl (15 Mℓ) , ,
 / (9:1) (E)-
 (3R,5S)-7-[2- -4-(4- -) -3-]-3,5- -6- ((S)-1- -
)- tert- -
 (E)-(3R,5S)-7-[2- -4-(4- -) -3-]-3,5- -6- ((S)-1- -
 -)- (1.197 g) tert- - (10 Mℓ) , (4 Mℓ) 가
 , 가
 0 5 , 2 ,
 (5 Mℓ) , 40 (E)-(3R,5S)-7-[2- -4-(4-
 -) -3-]-3,5- -6- ((S)-1- -)- . ¹H-NMR
 1:1 tert- - . M.p.:
 57 76 ; [α]_D²⁰ = -27.0° (CHCl₃, c=1); MS (ES+, m/z): 547([M+Na]⁺), 525 (MH⁺, 100
 %); IR(KBr): 3479, 3296, 2977, 1642, 1557, 1513, 1490, 1215, 1116, 1068, 763, 698 cm⁻¹ ;
 : C₃₃H₃₃FN₂O₃ + C₅H₁₂O () 74.48 (74.47) % C, 7.40 (7.30) % H, 4.57 (4.6
 4) % N, 3.10 (3.13) % F.

(E)-(R)-7-[2- -4-(4- -)- -3-]-3-
 -5- -6- ((S)-1- -)- (E)-(3R,5S)-7-[2- -4-(4-
 -) -3-]-3,5- -6- ((S)-1- -)-
 (30.26 g) , 가 4
 (54.85 g) (1877 Mℓ) 가 , -78 가
 (54.85 g, 548.4 mmol) 15 -78 가
 (290.7 g, 556 mmol) 2.5 (488 Mℓ) (581 Mℓ) (E)-(R)-7-[2-
 -78 1 (7346 Mℓ) 가 , (4610 Mℓ) (92.15 g) 가
 (2 x 3150 Mℓ) , (2 x 315
 0 Mℓ)
 (630 Mℓ) , 50 가 (60.907 g) 174.0
 2 g 35 % , 1790 mmol) 45 50 가 , 가
 45 50 (3980 Mℓ) 가 , (2390 Mℓ)
 Na₂SO₃ (2850 Mℓ) 118 g) , 5 Na
 , NaCl (2 x 2390 Mℓ) ,
 (349 g) t- - (706 Mℓ)
 , 0 .30 0 , 30 가 ,
 15 0 ,3 25 , 2
 , 40 (E)-(3R,5S)-7-[2- -4-(4- -) -3-]-
 3,5- -6- ((S)-1- -)- t- -
 58 69 . HPLC , 99.89 % syn-(3R,5S)- 0.11 %
 -(3R,5R)-

h)

(Cellflock), 1.0 g) 가 , 30
 (E)-(3R,5S)-7-[2-(4-(4-)-3-]-3,5- (0.260 g,
 6.5 mmol) 가 , (2.55 g, 6.05 mmol) (40.5 Mℓ) (0.399 g, 3.49 mmol)
 가 , (2 Mℓ) 4 2
 0 25 , 2 15 17 , 10.6 % (w/w) (E)-(3
 R,5S)-7-[2-(4-(4-)-3-]-3,5- -6- ,
 . [α]_D²⁰ = +22.92° (1:1 / , c= 1). X- A가 . (3S,
 5R) 0.05 % (HPLC HPLC
 99.7 % , 0.09 % (3R,5R) (3S,5S)
 (3R,5R)) 0.05 %

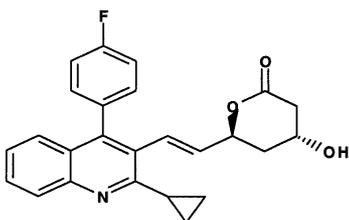
J)



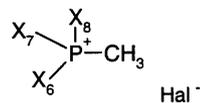
(E)-(3R,5S)-7-[3-(4-)-1- -1H- -2-]-3,5- -6-
 (E)-(3R,5S)-7-[2- -4-(4-)-3-]-3,5- -6-
 가 , (E)-(3R,5S)-7-[3-(4-)-1-
 -1H- -2-]-3,5- -6- ((S)-1-)-
 가 , 60 70 가 .
 5 , (E)-(3R,5S)-7-[3-(4-)-1- -1H- -
 2-]-3,5- -6-
 . []₂₀ = -20° (c= 0.8). - HPLC ()
) IR MS , (E)-(3R,5S)-7-[3-(4-
 -)-1- -1H- -2-]-3,5- -6- ([Tempkin et al., Te
 trahedron 1997, 53, 10659-10670])

, (E)-(3R,5S)-7-[3-(4-)-1- -1H- -2-]-3,5- -6-
 NaOH (4R,6S)-6-{(E)-2-[3-(4-)-1- -1H- -2-]-
 -2- }-4-

k)

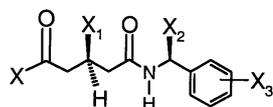


(4R,6S)-6-{(E)-2-[2- -4-(4-)-3-]- }-4-
 -2-



(
 X_4 X_5 C_1-C_7- $-C_1-C_7-$,
 X_6, X_7, X_8 CF_3 C_1-C_7 , C_1-C_7 , C_2-C_8 - ,
 Hal-)

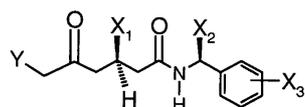
< IIIc >



(
 X , - 2 ,
 X_1 ,
 X_2 C_1-C_7 ,
 X_3 , CF_3 C_1-C_7 , C_1-C_7 , C_2-C_8 - , ,
) ;

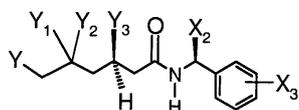
(b) , , III d III e

< III d >



(
 X_1, X_2, X_3 ,
 Y $(X_4 O)(X_5 O)P(=O)-$ $(X_6)(X_7)(X_8)P + Hal-$,
 X_4, X_5, X_6, X_7, X_8 Hal-)

< III e >



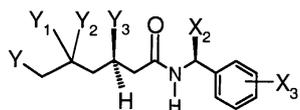
(
 ,

X_2, X_3 Y ,
 Y_1 , Y_2 , Y_3 , Y_1 Y
 Y_3 syn- ;

Y_1 Y_3 -O-Alk-O- , Alk C₁-C₇ , Y_2 , Y_1 Y_3 syn-
);

(c) , IIIe IIIf IIIg
 ----- 가 -CH=CH- ----- 가 -CH₂-CH₂- ,
 IIIg

< IIIe >



(,
 X_2, X_3 Y ,
 Y_1 , Y_2 , Y_3 , Y
 Y_1 Y_3 syn- ;

Y_1 Y_3 -O-Alk-O- , Alk C₁-C₇ , Y_2 , Y_1 Y_3 syn-
 ;

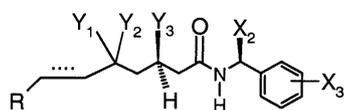
Y_1 Y_2 , Y_3 , III d
)

< IIIf >

R-CH(=O)

(,
 R)

< IIIg >

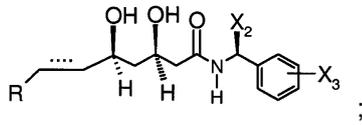


(,
 R ,
 X_2, X_3, Y_1, Y_2 Y_3 ,
 ----- -CH₂-CH₂- -CH=CH-);

(d) Y_1 Y_3 , Y_1 Y_3 syn , Y_1 Y_3 -O-Alk-O-
 , Alk C₁-C₇ , Y_1 Y_3 syn ; Y_1 Y_3 III g
 , Y_2

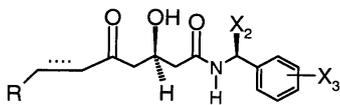
-----가 -CH=CH- () IIIh, IIIh -----가 -CH₂-CH₂- IIIh

< IIIh >



(e) Y₁, Y₂가 =O Y₃ (X₁) IIIg IIIh IIIi, II

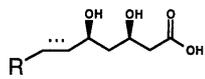
< IIIi >



(R, X₂, X₃ ----- 가);

(f) IIIh I 가

< I >

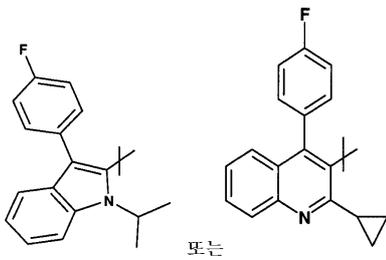


(----- -CH₂-CH₂- -CH=CH- R);

(g) I, I la Ib I la Ib, I

2.

1 -----가 -CH=CH- R



3.

1 IIIh, 2 IIIi, X₂가 X₃, IIIc, IIId, IIIe, IIIg,

4.

1, 2, X가 N-C₁-C₇ -N-C₁-C₇ - IIIc

5.

1, 2, X₁ tert-, tert-, - - - IIIc, IIId, IIIe, IIIg, IIIh